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EXAMINER	
GROSS, CHRISTOPHER M	
ART UNIT	**PAPER NUMBER**
1636	

NOTIFICATION DATE	DELIVERY MODE
11/10/2011	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/802,249	MAURITZ ET AL.	
	Examiner	Art Unit	
	CHRISTOPHER M. GROSS	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 August 2011*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ An election was made by the applicant in response to a restriction requirement set forth during the interview on _____; the restriction requirement and election have been incorporated into this action.

4)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

5)☒ Claim(s) *1-3,13 and 15-22* is/are pending in the application.

5a) Of the above claim(s) _____ is/are withdrawn from consideration.

6)☐ Claim(s) _____ is/are allowed.

7)☒ Claim(s) *1-3, 13, and 15-22* is/are rejected.

8)☐ Claim(s) _____ is/are objected to.

9)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

10)☐ The specification is objected to by the Examiner.

11)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

12)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Responsive to communications entered 8/8/2011
Claims 1-3, 13, and 15-22 are pending.
Claims 1-3, 13, and 15-22 are under consideration.

Priority

This application was filed 3/17/2004 and application claims foreign priority to EPO 03006098.2 (3/19/03). Receipt is as previously acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Withdrawn Objection(s) and/or Rejection(s)

The rejection of claim(s) 15-22 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is hereby withdrawn in view of applicant's amendments.

Maintained Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 13, 15-22 are rejected under 35 U.S.C. 102(b) as being anticipated by **Agris** (US Application Publication 20020045167; of record).

The claimed subject matter per claim 1 is drawn to a quality control method for achieving complete deprotection of protected reactive groups in on-chip synthesis of a biopolymer array, the method comprising
(a) synthesizing a plurality of biopolymer species on an array from monomeric or oligomeric nucleotide building blocks comprising detectable protecting groups coupled directly to amino groups of the nucleotide building blocks, wherein the detectable protecting groups remain coupled until synthesis of the biopolymer array is complete,
(b) taking one or more steps to cleave the detectable protecting groups,
(c) determining a degree of deprotection by detecting any of the detectable protecting groups remaining on the array after cleavage, and
(d) repeating steps (b) and (c) until the detectable protecting groups are no longer detected, indicating that complete deprotection is achieved,
wherein the quality control method is performed entirely on-chip and wherein the synthesized biopolymer are not destroyed by practice of the quality control method

Agris teaches, throughout the document and especially the abstract and paragraphs 0002-0006 and figure 11, antibodies specific for oligonucleotide protecting groups applied toward detecting incomplete deprotection on microarrays.

In paragraphs 0154-0157, Agris suggest the antibodies may be used on chips such as developed by Fodor, etc. which are made by synthesizing a plurality of biopolymer species on an array from monomeric or oligomeric nucleotide building blocks comprising detectable protecting groups coupled directly to amino groups of the nucleotide building blocks, wherein the detectable protecting groups remain coupled until synthesis of the biopolymer array is complete, as set forth in claim 1a. In figure 8, Agris takes a step to cleave detectable protecting groups such as Bz and ipr-Pac, as set forth in claim 1b; with said antibodies, determine the degree of deprotection by detecting

any of Bz and ipr-Pac remaining on an array after cleavage, as set forth in claim 1c; and re-deprotect until the detectable protecting groups are no longer detected, indicating that complete deprotection is achieved, as set forth in claim 1d. Antibody binding does not destroy the oligonucleotides as set forth in the second wherein clause of claim 1.

In paragraph 0037, Argis et al indicate the method may be used with fluorescent protecting groups such as fluorenylmethoxycarbonyl, reading on claim 2.

Said oligonucleotide reads on the nucleic acid (elected species) of claim 13.

Argis teaches various protected monomeric building blocks in paragraphs 0035-0077 and in particular uses (5'-dimethoxytrityl-N-phenoxyacetyl-2'-deoxyAdenosine,3'-[(2- cyanoethyl)-(N,N-diisopropyl)]-phosphoramidite in paragraph 0177, which reads on claims 15-22 formula I when R1 is DMT; R2 is H; B is adenine; R6 is a 2 cyanoethyl phosphoramidite; L is -C(O)-R, reading on claims 15-22.

***

Please note that the above rejection has been modified from the original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Response to Arguments

In the remarks entered 8/8/2011 applicant argues not all elements are taught.

Applicant's arguments have been fully considered but they are not deemed persuasive for the following reasons.

On p 6-9 the remarks argue that in paragraph 0162, Agris et al do not teach step (d) of claim 1 "repeating steps (b) and (c) until the detectable protecting groups are no longer detected, indicating that complete deprotection is achieved" which the remarks assert was indicated in the last office action.

In reviewing the last office action, it does not appear to point to paragraph 0162, but rather figure 8. In this vein, applicant's attention is respectfully invited to paragraph 0021 which describes the experiments shown in therein:

> FIG. 8 shows a blind study **demonstrating the detection of remaining protecting groups** in commercial samples. dA-dC oligos were analyzed with anti-Bz mAb (A) and dG-dT oligos were analyzed with anti-ipr-Pac mAb (B). The oligo dA-dC samples from companies #2 and #6 were tested in higher amounts to confirm the presence of the Bz protecting group (C). In addition, **the samples were treated to remove the remaining protecting groups using a standard protocol**. The oligo dG-dT samples were assayed for the ipr-Pac protecting groups (D). **The samples were re-treated to remove remaining protecting groups and re-analyzed as in (C).** Emphasis Added.

Such as shown in figure 8C right panel columns samples #6* and #2* were re-deprotected (re-treated) until such time as a spot is not detected (i.e. anti-Bz and anti-ipr-Pac mAbs do not bind indicating complete deprotection has been achieved).

The paragraph bridging pp 8-9 of the remarks asserts using the antibodies of Agris would impose degrees of complexity on the synthetic protocol with regard to non-specific binding of fluorescently labeled protecting group antibodies of Agris et al.

In this vein in so far as the remarks contend that the skilled artisan would not be motivated to use the antibodies of Agris et al, it is noted the foregoing rejection is for anticipation not obviousness, for which motivation is not a factor. Secondly, assuming *arguendo* the rejection was indeed for obviousness, this is not found persuasive

because the arguments of counsel cannot take the place of evidence in the record. *In re Schulze*,346 F.2d 600, 602, 145 USPQ 716, 718 (CCPA 1965); *In re Geisler*, 116 F.3d 1465, 43 USPQ2d 1362 (Fed. Cir. 1997) ("An assertion of what seems to follow from common experience is just attorney argument and not the kind of factual evidence that is required to rebut a prima facie case of obviousness.") (see MPEP 2145 I.) In the instant case, *despite the fact that Agris et al explicitly state that the antibodies are well suited toward testing of microarrays* (see paragraphs 0154-0157 as mentioned in the rejection above), applicant's counsel asserts fluorescently labeled antibodies non-specifically bind to microarrays but counsel does not provide objective evidence establishing said assertion as a fact. In fact, as explicitly cited by Agris et al in paragraph 0156, evidence provided in US patent 5445934 (to Fodor et al) in column 3 lines 39-61 for instance, demonstrates fluorescently labeled antibodies have been successfully employed in the on DNA microarray art for some fourteen years since the filing date of the present application. Finally, in response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (i.e., a quality control method for chips with surfaces which adventitiously bind fluorescently labeled antibodies) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Maintained Claim Rejection(s) - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 13, 15-22 and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over **Agris** (US Application Publication 20020045167; of record) in view of **Nagaich et al** (1989 Nucleic Acids Research 17: 5125-5134)

Agris is relied on as above.

Agris does not teach stilbene protecting groups, such as set forth in claim 3.

Nagaich et al teach, throughout the document and especially figure 1, stilbene protecting groups (elected species) for cytidine, adenine and guanine nucleosides reading on claim 3.

It would have been *prima facie* obvious for one of ordinary skill in the art, at the time the claimed invention was made to utilize the stilbene protecting groups of Nagaich et al in making microarrays and analysis of deprotection thereof in the manner of Agris.

One of ordinary skill in the art would have been motivated to utilize the stilbene protecting groups of Nagaich et al in making microarrays and analysis of deprotection thereof in the manner of Agris for the advantages of: (i) stability of the monomers; (ii) milder conditions for deprotection resulting in negligible side products during synthesis; and (iii) above all greater hydrophobicity, as explicitly noted by Nagaich et al in last sentence of the abstract.

One of ordinary skill in the art would have had a reasonable expectation of success in applying the stilbene protecting groups toward preparing and analyzing biochips in the manner of Agris since each reference is directly concerned with nucleotide exocyclic amine protection, thus the teachings of Nagaisch et al fall squarely in the scope of technology of interest to Agris.

Response to Arguments

In the paragraph bridging pp 11-12 of the 8/8/2011 remarks asserts the claimed method constitutes the simplest and most efficient method for providing completely deprotected microarrays due to the selection of protecting groups currently claimed.

Applicant's arguments have been fully considered but they are not deemed persuasive for the following reasons.

In response to applicant's argument that the claimed combination of oligonucleotide protecting groups may allegedly be more easily monitored during nucleic acid synthesis, the fact that applicant has recognized another advantage which would flow naturally from following the suggestion of the prior art cannot be the basis for patentability when the differences would otherwise be obvious. See *Ex parte Obiaya*, 227 USPQ 58, 60 (Bd. Pat. App. & Inter. 1985). Furthermore, in accordance with MPEP 2141 section III (C) citing *KSR International Co. v. Teleflex Inc. (KSR)*, 550 U.S. 1398, 1397 choosing from a finite number of identified, predictable solutions (e.g. exocyclic amine protecting groups) with a reasonable expectation of success is obvious.

Other than the above, applicant does not offer further arguments regarding the above obviousness rejections beyond what was set forth with regard to the 35 U.S.C. § 102 rejection, above. To the extent that Applicant is merely repeating their previous argument, the Examiner contends that those issues were adequately addressed in the above sections, which are incorporated in their entireties herein by reference.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CHRISTOPHER M. GROSS whose telephone number is (571)272-4446. The examiner can normally be reached on M-F 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571 272 0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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